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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,925	07/30/2000	ELIAS GEORGES	641050.90013	9902

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EXAMINER
ROBINSON, HOPE A

ART UNIT	PAPER NUMBER
1653	12

DATE MAILED: 04/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/529,925	Georges et al.
Examiner	**Art Unit**
Hope Robinson	1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 5, 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *6, 7, 15-27, and 30-36* is/are pending in the application.

4a) Of the above, claim(s) *6, 7, 24-27, and 30-33* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *15-23 and 34-36* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Applicant's response to the Office Action mailed May 4, 2001 in Paper No. 11 on November 5, 2001 is acknowledged.

2. Claims 34-36 have been added. Claims 15, 16, 17, 18, 19, 22 and 23 have been amended. Claims 6-7, 15-27 and 30-36 are pending. Claims 15-23 and 34-36 are under examination.

3. The following grounds of rejection are or remain applicable :

Oath/Declaration

4. The Oath/Declaration remains objected to because it is difficult to read the names of the inventors. A substitute Oath/Declaration which clearly sets forth the inventors' names is required. It is noted that Paper No: 11 indicates the submission of a substitute Oath, however none was received.

Abstract

5. The Abstract remains objected to because the abstract submitted has the headings : "Version with markings to show changes made" and "In the specification". In addition, the Inventor with Bibliographic type of information is listed along with the Examiner's information. The abstract also was not submitted on a separate page. Applicant is reminded that the abstract of the disclosure needs to commence on a separate sheet in accordance with 37 CFR 1.52(b)(1).

A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 15-23 and 34-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 is indefinite because the claim recites "modulates/modulator"and it is unclear if "modulates" means increase or decrease as only one term should be recited in the claim (see also claim 34). The claim is further indefinite regarding the conditions, it is difficult to determine what "drug" the affecting compound will be incubated with or not according to item (a) of the claim. Claim 15 is also indefinite in that the claim fails to clearly delineate an assay which appears required to identify the Annexin-based MDR-affecting compound. Further, the claim does not set forth a method step to demonstrate how to "assess" the effect of the compound or to demonstrate the end point of the method. The dependent claims are included in this rejection.

Claim 17 remains indefinite because the claim recites "small molecule". This terminology is not specific as to the identity of the material proposed (see also claim 20).

Claim 20 remains indefinite because the claim recites a "method of modulating Annexin-based MDR in a cell" and does not recite whether modulation is up or down. The dependent claims are included in this rejection.

Claim 34 is indefinite as the claim depends from a canceled claim.

7. Applicant's amendment filed November 5, 2001 has been considered, but was not persuasive, thus the rejections under 35 U.S.C. 112, second paragraphs remains. Applicant contends that the terminology "small molecule" in claims 17 and 20 is well known and is clear to a person of ordinary skill in the art. Applicant also states that "the examiner is referred to page 30, lines 3-7 which relates to "small molecule". The specification on page 30 discloses that "these

results suggest that small molecules find utility in the context of the present invention". There is no description as to what is considered to be "small molecules". Furthermore, the limitations of the specification cannot be read into the claims. Applicant also contends that the terminology "small molecule" is well known, well known by whom? What does applicant mean by small molecule, what is encompassed in this to satisfy the metes and bounds of the claim.

Regarding the terminology used in the claims of "modulator or modulating", applicant states that the term is used to cover both an increase in resistance and a decrease in resistance of a cell to Annexin-based MDR. It is further stated that the bi-directional nature of this modulation is clearly supported throughout the disclosure and it is believed that the recitation is clear and distinct. The issue raised is not one of support but that the term as recited in the claim is indefinite because it is ambiguous which applicant admits by stating that it is "bi-directional" and intended to mean "increase and decrease". The two opposing actions cannot be recited in the same claim and as the term modulate has two different meaning applicant needs to amend the claims to recite either increase or decrease, not both.

The response argues that the amendments to claim 15 renders the rejection moot. However, claim 15 as amended still does not recite an end point in the method steps, an assay to achieve the assessing or how to assess, and does not define the candidate compound or the drug that is to produce the desired effect. Thus, the method has an unspecified compound and drug that is being used to identify compounds that modulate Annexin-based multidrug resistance. As the arguments presented are not convincing for the reasons stated above the rejection remains.

Claim Rejections - 35 U.S.C. § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 15 and 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al. (Biochemical and Biophysical Research Communications, vol. 236, pages 483-488, 1997) based on the disclosure which states that P-40 is Annexin I and that the invention relates to the identification of Annexins (I-XI, also referred to herein as P-40 and P-40 homologs (see page 4 of the specification).

Wang disclose a method that identifies a protein that mediates drug resistance to anticancer drugs. Wang also disclose a method that was used to isolate a monoclonal antibody (IPM96) which recognized a protein (P-40) co-expressed with P-glycoprotein in several resistant cell lines. Wang further discloses that over expression of P-40 in multidrug resistant cells may be important in the expression of the drug resistance phenotype (see pages 483-485).

Additionally, Wang disclose a method comprising the binding of IMP96 to P-40 in MCF-7/Adr cells (see Figure 1) and demonstrates that P-40 (Annexin I) confers resistance to Taxol and Adriamycin (see Table 1). Wang further discloses that the over expression of P-40 in paclitaxel or cis-platinum selected cell lines, in the absence of a detectable level of P-gp or MRP supports the

notion that P-40 alone may confer resistance to cytotoxic drugs (see page 486). Wang also disclose that P-40 could modulate an MDR phenotype indirectly, by stating that P-40 may be a component of the apoptosis signaling pathway. Moreover, Wang discloses that changes in the levels or functions of proteins involved in the signaling of apoptosis can confer an MDR phenotype on tumor cells (see page 487).

Therefore, Wang anticipates the claimed invention as Wang identifies a compound (P-40) that affects Annexin-based MDR in a cell in the presence of a drug (Adriamycin and Taxol) and assessed the effect of said compound as claimed in the present application. Further, Wang discloses a method that utilizes an antibody to Annexin and a compound that modulates Annexin based MDR in a cell as the present application discloses that P-40 and Annexin are equivalent.

9. With regard the rejection under 35 U.S.C. 102(b), the rejection remains because claim 15 does not recite P-40, the claim broadly recites "a method of identifying a compound that modulates Annexin-based multidrug resistance (MDR) in a cell...". The Wang reference is relevant because page 487 teaches that over expression of P-40 was found in MDR cells and that P-40 can modulate an MDR phenotype. Thus, Wang anticipates the claimed invention. It is noted that applicant cited references such as Sugimoto et al., Schinkel et al., Kool et al. and Bleik et al., which have not been submitted for consideration or is of record in the present application on a PTO 1449 form. Therefore, applicant's statements are not convincing. Applicant needs to

provide the references and an Information Disclosure Statement for the references to be considered.

Applicant's contention that Wang neither teaches nor suggests the direct role of Annexin in multidrug resistance is not persuasive as the claims do not recite that. Furthermore, the reference teaches modulation of MDR phenotype via P-40 which is disclosed in the present application as Annexin I. In addition, the present specification discloses that the invention relates to the identification of Annexins (I-XI, also referred to herein as P-40 and P-40 homologs (see page 4 of the specification). Therefore, the rejection remains.

Conclusion

10. Applicant's amendment necessitated the new/modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Hope A. Robinson whose telephone number is (703)308-6231. The Examiner can normally be reached on Monday - Friday from 9:00 A.M. to 5:30 P.M. (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor Christopher S.F. Low, can be reached at (703)308-2923.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703)308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-4242. Please affix the Examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope A. Robinson, MS

Patent Examiner

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER